b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.

67. A method for inhibiting human TNFα activity comprising contacting human TNFα with an antibody such that human TNFα activity is inhibited, wherein the antibody is an isolated human antibody, or an antigen binding portion thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2.

68. A method for inhibiting human TNFα activity in a human subject suffering from a disorder in which TNFα activity is detrimental, comprising administering to the human subject an antibody such that human TNFα activity in the human subject is inhibited, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human TNFα with a K_d of 1 x 10^{-8} M or less and a K_{off} rate constant of 1 x 10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1 x 10^{-7} M or less.

69. A method for inhibiting human TNFα activity in a human subject suffering from a disorder in which TNFα activity is detrimental, comprising administering to the human subject an antibody such that human TNFα activity in the human subject is inhibited,

wherein the antibody is an isolated human antibody, or antigen-binding portion thereof, with the following characteristics:

a) dissociates from human TNFα with a K_{off} rate constant of 1×10^{-3} s^{-1} or less, as determined by surface plasmon resonance;

b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.

70. A method for inhibiting human TNFα activity in a human subject suffering from a disorder in which TNFα activity is detrimental, comprising administering to the human subject an antibody such that human TNFα activity in the human subject is inhibited, wherein the antibody is an isolated human antibody, or an antigen binding portion thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2.

C2 71. **(Amended)** A method for inhibiting human TNFα activity in a human subject suffering from a disorder in which TNFα activity is detrimental, comprising administering to the human subject an antibody such that human TNFα activity in the human subject is inhibited, wherein the antibody is D2E7.

C3 73. **(Amended)** The method of any one of claims 68, 69, 70, and 71 wherein the disorder is an autoimmune disease

63

C

9 ~~76.~~ **(Amended)** The method of any one of claims ~~68, 69, 70,~~ and ~~71~~ 4 5 6 7 wherein the disorder is an infectious disease.

10 ~~77.~~ **(Amended)** The method of any one of claims ~~68, 69, 70,~~ and ~~71~~ 4 5 6 7 wherein the disorder is transplant rejection or graft-versus-host disease.

11 ~~78.~~ **(Amended)** The method of any one of claims ~~68, 69, 70,~~ and ~~71~~ 4 5 6 7 wherein the disorder is a malignancy.

CA ~~79.~~ **(Amended)** The method of any one of claims ~~68, 69, 70,~~ and ~~71~~ 4 5 6 7 wherein the disorder is a pulmonary disorder.

13 ~~80.~~ **(Amended)** The method of any one of claims ~~68, 69, 70,~~ and ~~71~~ 4 5 6 7 wherein the disorder is an intestinal disorder.

14 ~~81.~~ **(Amended)** The method of any one of claims ~~68, 69, 70,~~ and ~~71~~ 4 5 6 7 wherein the disorder is a cardiac disorder.

Please add the following new claims:

15 ~~83.~~ (New) The method of any one of claims ~~68, 69, 70,~~ and ~~71~~ 4 5 6 7 wherein the disorder is sepsis.

C5 16 ~~84.~~ (New) The method of claim ~~83,~~ 15 wherein the antibody is administered to the human subject together with the cytokine interleukin-6 (IL-6) or is administered to a human subject with a serum or plasma concentration of IL-6 above 500 pg/ml.

17 ~~85.~~ (New) The method of any one of claims ~~68, 69, 70,~~ and ~~71~~ 4 5 6 7 wherein the disorder is rheumatoid arthritis.

64

C

18 86. (New) The method of any one of claims 68, 69, 70, and 71 wherein the disorder is rheumatoid spondylitis.

19 87. (New) The method of any one of claims 68, 69, 70, and 71 wherein the disorder is osteoarthritis.

20 88. (New) The method any one of claims 68, 69, 70, and 71 wherein the disorder is gouty arthritis.

21 89. (New) The method of any one of claims 68, 69, 70, and 71 wherein the disorder is an allergy.

22 90. (New) The method of any one of claims 68, 69, 70, and 71 wherein the disorder is multiple sehlerosis. sclerosis

23 91. (New) The method of any one of claims 68, 69, 70, and 71 wherein the disorder is autoimmune diabetes.

24 92. (New) The method of any one of claims 68, 69, 70, and 71 wherein the disorder is autoimmune uveitis.

25 93. (New) The method of any one of claims 68, 69, 70, and 71 wherein the disorder is nephrotic syndrome.

26 94. (New) The method of any one of claims 68, 69, 70, and 71 wherein the disorder is inflammatory bone disorders.

27 95. (New) The method of any one of claims 68, 69, 70, and 71 wherein the disorder is bone resorption disease.

28 96. (New) The method of any one of claims 68, 69, 70, and 71 wherein the disorder is alcoholic hepatitis.

29 97. (New) The method of any one of claims 68, 69, 70, and 71 wherein the disorder is viral hepatitis.

30 98. (New) The method of any one of claims 68, 69, 70, and 71 wherein the disorder is coagulation disturbances.

31 99. (New) The method of any one of claims 68, 69, 70, and 71 wherein the disorder is burns.

32 100. (New) The method of any one of claims 68, 69, 70, and 71 wherein the disorder is reperfusion injury.

15 Cont 33 101. (New) The method of any one of claims 68, 69, 70, and 71 wherein the disorder is keloid formation.

34 102. (New) The method of claim any one of claims 68, 69, 70, and 71 wherein the disorder is scar tissue formation.

35 103. (New) The method of any one of claims 68, 69, 70, and 71 wherein the disorder is pyrexia.

36 104. (New) A method for treating a subject suffering from a disorder in which TNFα activity is detrimental, comprising administering to the subject an antibody such that the disorder is treated, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human TNFα with a K_d of 1 x 10^{-8} M or less and a K_{off} rate constant of 1 x 10^{-3} s^{-1} or less, both determined by surface plasmon

resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} M or less.

37

105. (New) A method for treating a subject suffering from a disorder in which TNFα activity is detrimental, comprising administering to the subject an antibody such that the disorder is treated, wherein the antibody is an isolated human antibody, or antigen-binding portion thereof, with the following characteristics:

a) dissociates from human TNFα with a K_{off} rate constant of 1×10^{-3} s^{-1} or less, as determined by surface plasmon resonance;

b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

C5

c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.

38

106. (New) A method for treating a subject suffering from a disorder in which TNFα activity is detrimental, comprising administering to the subject an antibody such that the disorder is treated, wherein the antibody is an isolated human antibody, or an antigen binding portion thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2

39

107. (New) A method for treating a subject suffering from a disorder in which TNFα activity is detrimental, comprising administering to the subject an antibody such that the disorder is treated, wherein the antibody is D2E7.

67

C

108. (New) The method of any one of claims 104, 105, 106 and 107, wherein the disorder is an autoimmune disease.

109. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is an infectious disease.

110. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is transplant rejection or graft-versus-host disease.

111. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is a malignancy.

112. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is a pulmonary disorder.

113. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is an intestinal disorder.

114. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is a cardiac disorder.

115. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is sepsis.

116. (New) The method of claim 115, wherein the antibody is administered to a human subject together with the cytokine interleukin-6 (IL-6) or is administered to a human subject with a serum or plasma concentration of IL-6 above 500 pg/ml.

117. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is rheumatoid arthritis.

118. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is rheumatoid spondylitis.

119. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is osteoarthritis.

120. (New) The method any one of claims 104, 105, 106 and 107 wherein the disorder is gouty arthritis.

121. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is an allergy.

122. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is multiple ~~schlerosis~~ sclerosis.

123. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is autoimmune diabetes.

124. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is autoimmune uveitis.

125. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is nephrotic syndrome.

126. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is inflammatory bone disorders.

127. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is bone resorption disease.

128. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is alcoholic hepatitis.

129. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is viral hepatitis.

130. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is coagulation disturbances.

131. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is burns.

132. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is reperfusion injury.

133. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is keloid formation.

134. (New) The method of claim any one of claims 104, 105, 106 and 107 wherein the disorder is scar tissue formation.

135. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is pyrexia.

136. (New) The method of any one of claims 68, 69, 70, 71, 104, 105, 106 and 107 wherein the isolated human antibody is combined with a pharmaceutically acceptable carrier.

137. (New) The method of claim 68, 69, 70, 71, 104, 105, 106 and 107 wherein the isolated human antibody is administered with at least one additional therapeutic agent.

138. (New) The method of any one of claims 104, 105, 106 and 107 wherein the subject is human.

139. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is septic shock.

140. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is endotoxic shock.

141. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is gram negative sepsis.

142. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is toxic shock syndome.

143. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is malaria.

144. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is meningitis.

145. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is cachexia.

146. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is AIDS.

147. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is bacterical meningitis.

148. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is AIDS-related complex (ARC).

149. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is cytomegalovirus infection secondary to transplantation.

150. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is fever or myalgias due to infection ~~and cachexia secondary infection.~~

151. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is allograft rejection.

152. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is stimulating tumor growth.

153. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is enhancing metastatic potential and mediating cytotoxicity in malignancies.

154. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is inhibiting tumor growth or metastasis.

155. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is adult respiratory distress syndrome.

156. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is shock lung.

89 157. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is chronic pulmonary inflammatory disease.

90 158. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is pulmonary sarcoidosis.

91 159. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is pulmonary fibrosis.

92 160. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is pulmonary silicosis.

93 161. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is inflammatory bowel disorder.

94 162. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is idiopathic inflammatory bowel disease.

95 163. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is Crohn's disease.

96 164. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is ulcerative colitis.

97 165. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is ischemia of the heart.

98 166. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is heart insufficiency.

99 167. (New) The method of any one of claims 104, 105, 106 and 107 wherein the disorder is hepatitis.

74

C